REMARKS

Docket number

Please change the attorney docket number to 2119-4263 (BB1129USPCT) on all future correspondence.

Status of Claims/Amendments

Claims 42-56 are pending in the instant application with Claim 42 being the sole independent claim. Claims 42-44 and 54 are currently amended.

Claim 42 is amended to identify the activity of the enzyme encoded by the claimed polynucleotides as glutamine amidotransferase HisHF. Support for this change is found throughout the specification as filed. For example, see Table 1 on page 6.

Claims 42-44 are amended to remove "V" from "Clustal V method of alignment" to conform with the disclosure as filed. Support for this change is found throughout the specification as filed. For example, see page 3, lines 30-33.

Claim 54 is amended to provide proper antecedent basis and to specify HisHF mutant as the histidine biosynthetic auxotroph. Support for this change can be found throughout the specification as filed. For example, see Example 9, page 30.

The specification is amended to correct certain clerical errors. Support for these changes is found, for example, on page 5, lines 20-35, and on page 22, lines 5-13.

Four pages of figures (Figures 1A-1D) are attached as replacement figures. The figures are amended to match the description, specifically that which is described in Example 9, page 30. Asterisks (*) are added to amino acids conserved among the impatiens and *Arabidopsis* glutamine amidotransferase HisHF polypeptides. The amino acids at positions 141, 246, 248,

403, 404, 447, 508, and 517 are boxed in black and written in white. The box around the amino acids at position 409 has been removed.

No new matter is introduced through these amendments.

Information Disclosure Statement

Applicants appreciate the Examiner's consideration of the Information Disclosure Statement, filed July 9, 2001 as indicated by return of a signed and initialed copy.

Sequence Listing

The Examiner requests clarification regarding the region of SEQ ID NO:1 that encodes SEQ ID NO:2. Nucleotides 2-1675 from SEQ ID NO:1 encode the polypeptide having SEQ ID NO:2. Nucleotides 1676-1678 form a stop codon.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 42-56 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim that which applicants regard as their invention. Claims 42, 43, 44, and 54 are amended as suggested in the Office Action. Withdrawal of the rejections under 35 U.S.C. § 112, second paragraph rejections is requested.

Rejection under 35 U.S.C. § 101 / 35 U.S.C. § 112, first paragraph: Utility

Claims 42-56 are rejected under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph for lack of utility and enablement (how to use). The rejection is due to the phrase "ornithine acetyltransferase." Claim 42 is amended to remove the phrase and replace it with

"glutamine amidotransferase (HisHF)". Applicants believe that the amendment fully addresses the rejection on the basis of utility. However, in order to advance prosecution, additional arguments are presented as they apply to the pending claims.

As noted by the Examiner, Table 4 of the specification shows SEQ ID NO:2 has 72.9% sequence identity to a glutamine amidotransferase, cited by the Examiner as "the closest prior art" (Office Action, page 3). The Examiner concedes that "SEQ ID NO:2 is a glutamine amidotransferase and not an ornithine acetyltransferase" (Office Action, page 3).

The Examiner argues that the utility requirements are not met because "Applicant does not disclose that SEQ ID NO:1 encodes a complete protein" since the sequence does not begin with the start codon for methionine. However, Applicants assert that although the amino acid sequence of SEQ ID NO:2 does not start with a methionine, the polypeptide encoded by the polynucleotide of SEQ ID NO:1 encodes an active glutamine amidotransferase HisHF polypeptide. As shown in the article by Fujimori and Ohta (considered by the Examiner in the IDS received by the USPTO July 9, 2001), the first 60 or so amino acids at the N-terminus of the *Arabidopsis thaliana* HisHF protein are not required for glutamine amidotransferase HisHF activity. In particular, a construct lacking them was capable of complementing a yeast His7 mutant. The start of this putative chloroplast transit peptide (CTP) is indicated in Figure 1 of the specification as filed. An extra copy of the reference is provided for the Examiner's convenience.

The Examiner further argues that there is no guidance as to where the catalytic domain is located. On the contrary, Figure 1 of the specification as filed also shows the location of the carbamoyl-phosphate synthase protein GATASE domain signature E motif 2 and the GATASE type 1 motif as well as the amino acids which, when mutagenized, affected HisHF enzyme activity. According to Example 9 of the specification as filed, Cys141, His246, Glu248,

Asp403, Lys404, Ser409, Asp447, Glu508, and Asp517 are required for glutamine amidotransferase HisHF activity. These amino acids are marked in Figure 1 where they are shown to be located in motifs conserved among all the glutamine amidotransferase HisHF polypeptides in the application.

Thus, the specification as filed shows that the polynucleotide having SEQ ID NO:1 encodes a polypeptide having glutamine amidotransferase HisHF activity. The specification as filed also shows the identification of amino acids essential for glutamine amidotransferase HisHF activity and the fact that these are located within conserved domains.

With respect to 35 U.S.C. § 112, first paragraph, removal of the phrase "ornithine acetyltransferase" and replacement of the phrase with "glutamine amidotransferase (HisHF)" should suffice to overcome the "how to use" rejection. The Examiner contends that neither the state of the art nor Applicant provided guidance as to which regions of the sequences must be retained for activity and which regions can tolerate mutations, particularly for those claims reciting less than 100% sequence identity (Office Action, page 4, paragraph 3). The Examiner concludes that "further guidance is necessary as to what changes would be tolerated" (Office Action, page 4, paragraph 3).

The Federal Circuit has held that a number of factors are considered in determining whether or not the disclosure is enabled. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Among the Wands factors are a consideration of the state of the art in the field of the invention, and the amount of guidance provided. As noted above, Figure 1 of the specification as filed also shows the location of the carbamoyl-phosphate synthase protein GATASE domain signature E motif 2 and the GATASE type 1 motif as well as the amino acids which, when mutagenized, effected HisHF enzyme activity. According to Example 9 of the

specification as filed, Cys141, His246, Glu248, Asp403, Lys404, Ser409, Asp447, Glu508, and Asp517 are required for glutamine amidotransferase HisHF activity. These amino acids are marked in Figure 1 where they are shown to be located in motifs conserved among all the glutamine amidotransferase HisHF polypeptides in the application.

Thus, the claimed sequences have utility and are enabled in the manner of use, and withdrawal of the 35 U.S.C. § 101 (utility) and 35 U.S.C. § 112, first paragraph, (how to use) rejections is kindly requested.

Rejection under 35 U.S.C. § 112, first paragraph: Written Description/New Matter

Claims 42-56 are rejected under 35 U.S.C. § 112, first paragraph for containing new matter due to the phrase "ornithine acetyltransferase." Claim 42 is amended to remove the phrase and replace it with 'glutamine amidotransferase (HisHF)". Applicants believe that the amendment fully addresses the rejection on the basis of new matter. Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph: Written Description

Claims 42-56 are rejected under 35 U.S.C. § 112, first paragraph for failure to comply with the written description requirement. The Examiner argues that SEQ ID NO:2 is only a partial gene sequence and does not contain a complete open reading frame encoding a complete protein. Therefore, the Examiner concludes that there is "insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine the complete structure of a gene encoding an ornithine acetyltransferase based upon the disclosure of a partial sequence, absent further guidance," (Office Action, page 6, first paragraph). Applicants

respectfully traverse, and note that claim 42 is amended to remove the phrase "ornithine acetyltransferase" and replace it with 'glutamine amidotransferase (HisHF)".

The Federal Circuit has interpreted the written description requirement of 35 USC 112, 1st paragraph as serving a teaching function, as a 'quid pro quo' in which the public is given "meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 959, 970 (Fed.Cir.2002). The Court held that functional descriptions of genetic material can, in some cases, meet the written description requirement if those functional characteristics are "coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Id.* at 964. To meet the requirement, the inventor must "describe the claimed invention so that one skilled in the art can recognize what is claimed." *Id.* at 968. In other words, the disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter puportedly described.

In the present case, the functional characteristic is having glutamine amidotransferase (HisHF) activity. One is able to test for the activity using known assays. For example, assays for complementing a yeast His7 mutant indicating restoration of activity are described in Fujimori and Ohta as discussed above.

With respect to structural information, some claims require at least 85% or more sequence identity with the disclosed sequence IDs. As sequence alignments are readily practiced in the art, one of ordinary skill is clearly put on notice whether or not a given sequence has at least 85%, or at least 90%, or at least 95% sequence identity with the disclosed sequence IDs. For example, Figures 1A-1D compare a number of sequences. This comparison demonstrates the sequences of the invention share highly conserved regions and the less conserved regions. One

skilled in the art would appreciate that the more highly conserved a residue is, the less likely that it could be modified and function maintained. No additional guidance is needed to allow one skilled in the art to predictably determine mutants, allelic variants, and glutamine amidotransferase HisHFs from other plants and organisms. Further, one skilled in the art recognizes that the sequences disclosed by the "closest prior art" as indicated by the Examiner (Office Action, page 3) share 72.9% sequence identity to a glutamine amidotransferase, and as such are outside the scope of the instant claims.

The Examiner has shown no reason why one of ordinary skill in the art would be unable to combine the functional and structural characteristics as disclosed in the specification in order to recognize the invention as claimed, and thereby meet the written description requirement. Therefore, Applicant respectfully requests withdrawal of the rejection.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all rejections and allowance of this application.

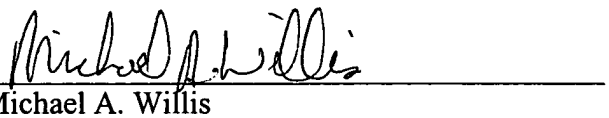
AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 2119-4267. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is

hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2119-4267. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: July 27, 2004 By: 

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